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A new morphometric method for the sella turcica and the hypophyseal fossa and its clinical relevance

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The sella turcica *and the hypophyseal fossa should be considered different entities, the latter being part of the former. Their morphology and dimensions correlate to some extent with those of the contained pituitary gland and have, for this reason, attracted the interest of anatomists and radiologists. With the application of MRI, however, these data are of limited use in the diagnosis of pituitary disorders, although they remain valuable with regard to a microsurgical approach to the hypophysis.*

The proposed morphometric method was applied to 20 dry skulls. We first made casts of the corresponding sellae. Their volumes were then measured by immersion. The frontal section of each hypophyseal fossa was obtained through its deepest point and magnified. The Cartesian co-ordinates of the contour of the section were used to evaluate the corresponding area and centroid. The volume of each fossa was finally obtained by the use of Pappus' theorem applied to solids of rotation.

The volumes of the sellae obtained as above ranged from 460 mm^3 to 1570 mm^3 with a mean value of 835 mm^3. These figures are comparable to those reported from previous authors. To our knowledge the method described has enabled a close approximation of the volumes of the hypophyseal fossae to be made for the first time. These volumes ranged from 24 mm^3 to 300 mm^3, with a mean value of 157 mm^3. Similar numerical methods might be applicable in vivo *by the use of MR imaging.*

Key words: Pituitary, hypophyseal, macroadenoma, empty sella, Pappus' theorem, solid of rotation

INTRODUCTION

The *sella turcica* (or simply sella) is an osseous structure closely related to the *hypophysis celebri* (or pituitary gland). Consequently, beyond its obvious anatomical importance, it has additional clinical significance, since its morphology reflects to some extent that of the pituitary gland itself.

The latter exhibits a great variability in shape that is, in turn, greatly enhanced by many kinds of neoplasias (microadenomas or macroadenomas), embryonic abnormalities (craniopharyngiomas) or other pathological states (empty sella syndrome, for instance).

According to classical anatomical texts (for example, [14, 17, 19]), the hypophyseal fossa is a cavity formed at the upper surface of the body of the sphenoid bone between the *tuberculum sellae* and the *dorsum sellae*. This structure thus constitutes the floor of the *sella turcica* and lodges the lower part

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of the hypophysis. Each lateral surface of the hypophysis is related to the homolateral *cavernous sinus*. The *diaphragma sellae* separate the anterior part of the *hypophysis celebri* from the optic chiasma and its posterior part from the *tuber cinereum*.

This description permits a clear distinction of the space limited by the bony parts of the sella (tuberculum, fossa and dorsum), the diaphragma and the cavernous sinuses, the depth and volume of which may be regarded as those of the entire sella and the hypophyseal fossa alone, the depth and volume of which are evidently much lower. We consider this elucidation to be necessary in view of the fact that some authors identify the hypophyseal fossa with the space beneath the diaphragma [9, 24].

Several anatomical studies reveal that the classical pattern of a concave shape of the hypophyseal fossa is frequently violated. Lang and Tisch-Rottensteiner [15] performed measurements on 71 dry skulls and reported that a normal round-shaped fossa is present in only 50% of the cases. In the rest of their sample they found a flat fossa in 15.5%, and a combination of a plateau with a concavity and/or a convexity in 31% of the specimens. They also remarked that the deepest point of the fossa is usually situated in its left side. On the other hand, Ouaknine and Hardy [16] made radiological observations in 266 patients and reported that the sellar floor was regular and symmetrical in 252 cases (94.7%) and asymmetrical or slightly oblique in 14 cases (5.3%).

The dimensions of the *sella turcica*, namely its length, width, depth and volume, have been measured by many other authors [7, 10, 21, 25]. The variability of the reported results is impressive. Thus the length of the sella varies between 5 mm and 16 mm, the width between 9 mm and 18 mm, the depth between 4 mm and 13 mm and the volume between 240 mm^3 and 1150 mm^3 [16].

The work of Renn and Rhoton [21] shows that the shape of the sella is influenced not only by the morphology of the hypophysis, but also by the existence and localisation of the venous sinuses that connect the cavernous sinuses crossing the midline and situated along the anterior, posterior or inferior surface of the pituitary gland.

Other investigators [13, 18] have described variations concerning the existence of osseous bridges between the clinoid processes that greatly affect the morphology of the sella, as well as its relation to the adjacent internal carotid artery.

Magnetic resonance imaging (MRI) has become the method of choice for the diagnosis of several types of lesion of the pituitary and its adjacent region. By means of MRI Baleriaux et al. [3] concluded that macroadenomas, meningiomas, craniopharyngiomas and cysts are more probable causes of deformation of the neighbouring bony structures. A correlation of pituitary disorders with MRI findings is given by Zucchini et al. [29].

Microsurgery is required for effective and safe treatment of various pituitary disorders such as macroadenomas or craniopharyngiomas. All the anatomical details concerning the possible variants of the sellar region must be taken into account by neurosurgeons in order to decide which approach (transfrontal, transethmoidal, transsphenoidal sublabian or endonasal) is to be chosen [21]. For this reason, neurosurgeons also perform anatomical studies on cadaveric specimens or dry skulls in order to obtain the additional information required [22].

The distance to be covered by the surgical endoscope during each of the above procedures constitutes an additional important factor. Accordingly, several studies have been performed on cadaveric specimens [8, 20, 23] in which this distance is measured using the deepest point or the centre of the sellar floor as a reference point.

Studies currently being performed have concerned the entire *sella turcica*. In our study, special regard was paid to the morphology of the hypophyseal fossa itself. An original method is presented, by which the geometrical features of the fossa were obtained and its deepest point was accurately determined. A comparison is made with previous findings concerning its dimensions and volume. The most frequent or clinically important abnormalities in the shape and volume of the pituitary gland and their eventual correlation with the morphology of the *sella turcica* are reviewed. A possible correlation of our method with MRI techniques is finally discussed.

MATERIAL AND METHODS

Our sample consisted of 20 dry skulls of variable dimensions, acquired from body donors of Greek origin. In each of these the dome had been removed and the middle cranial fossa had been revealed. A cast of the *sella turcica,* the space beneath the *diaphragma sellae* between the middle and the posterior clinoid processes, was obtained by the use of a dental silicon material (Primosil[R]). A pin was inserted into this material at the level (*l*) of the two lateral rims of the sella for the purpose of obtaining as accurately as possible the upper boundary of the hypophyseal fossa per se (Fig. 1).

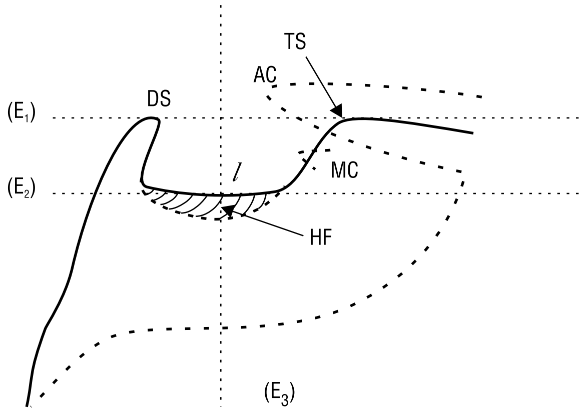

Figure 1. Schematic representation of a sagittal section through the middle of the *sella turcica*. TS — tuberculum sellae; AC — anterior clinoid; MS — middle clinoid; DS — dorsum sellae; HF — hypophyseal fossa; (E_1) — upper level of the cast; (E_2) — upper level of the fossa; (E_3) — line indicating the plane of the frontal section; *l* — the point of the lateral margin where the marking pin was inserted.

After the hardening of the silicon material, the solid cast representing the *sella turcica* was removed and its volume (defined as V_S) determined by immersion. Subsequently, we performed a frontal section through this cast, passing through the point of the maximal depth of the fossa. The contour of this section was drawn in a millimetre sheet (Fig. 2) and magnified 5 times (Fig. 3). A graph was thus obtained in which the beginning of the axes corresponded to the left margin of the fossa. The Cartesian co-ordinates (X.Y) were measured and recorded. X is the distance from both margins (at intervals of 0.5 mm) to the point corresponding to the maximal depth and Y is the respective depth.

The data obtained in this way enabled us to evaluate the area (A) of the section as well as to obtain a fairly good approximation of the volume (V) of the fossa.

If we consider that Y = f(x), the area is given by the formulae:

$$A = \int_0^{X_{max}} f(x)dx \ (1) \quad \text{or} \quad A = \sum_{i=1}^{n} Y_i \times 0.5 \ (2)$$

where $X_{max} = n \times 0.5$ mm (3)

In order to evaluate the volume V, we considered the fossa as a solid of rotation, in which Pappus' theorem (see, for example, [26]) may be applied. According to this theorem, the volume of rotation V_r is given by the formula:

$$V_r = 2\pi rA \ (4)$$

where A is the area of the rotating surface and r is the distance of its "centre of mass" (more correctly designated as "centroid") from the axis of rotation, provided that the latter is situated outside this surface.

In order to better approximate the volume, seeing that the maximal depth Y_{max} is not as a rule situated at the centre of the fossa, we divided the section into two parts: one on the left and one on the right of Y_{max} and considered the axis of rotation as passing through Y_{max}. Accordingly we set:

$$V_L = \pi r_L A_L \ , \quad V_R = \pi r_R A_R \ , \quad V = V_L + A_R \ (5)$$

The areas A_L and A_R are obtained with the help of (2) and (3). The radii of rotations were of course equal to:

$$r_L = X_{max,\,L} - Xm_L \quad \text{and} \quad r_R = X_{max,\,R} - Xm_R \ (6)$$

where Xm_L and Xm_R stand for the x-coordinates of the centres of mass (or "centroids") for each half, for which the general formula (see, for example, [28])

$$Xm = \frac{1}{A}\int_0^{X_{max}} x \bullet f(x) \bullet dx$$

$$\text{or} \quad Xm = \sum_{i}^{n} Xi \times Yi \times 0.5 \ (7)$$

was applied for each part.

The mathematical processing was carried out with the help of a PC-version of FORTRAN programming.

A statistical analysis of our data was made for the examination of an eventual correlation of the dimensions of the hypophyseal fossa with those of the corresponding skulls. In view of the small number of specimens (n = 20), we used non-parametric statistics to evaluate the correlation coefficient of the variables-parameters according to Spearman (see, for example, [5]), as well as the statistical trial known as the paired t-test (the Wilcoxon signed ranks test) for the testing of the differences between the variables L (length) and W (width) of the two anatomical entities. The chi-squared test was finally used to check whether the left preference of the position of maximal depth of the fossa was greater than the right in a statistically significant way.

RESULTS

The main results of our measurements and calculations are presented in Table 1.

The first column contains the serial number of each of our 20 specimens.

The second column contains information relative to the position of the maximal depth of the hypophy-

Table 1. Morphometric data concerning the *sella turcica* and the hypophyseal fossa for our sample consisting of 20 dry skulls. A: area (in mm^2) of a frontal section of the hypophyseal fossa through its maximal depth.
V_{DN} ($= 0.5 \times X_S \times X_T \times Y_{max}$) is the volume (in mm^3) of the fossa according to DiChiro and Nelson [10]. V_F is the same volume evaluated according to our method. V_S is the volume of the sella. Y_{max}, L_{fos} and W_{fos} (in mm) are respectively the maximal depth, the length and the width of the fossa. L_{scul} and W_{scul} represent (in mm) the length and width of the skull. The shapes of the fossa: C — concave, P — plateau. MV — mean values

No.	Position of max depth	Area A	Volume V_{DN}	Volume V_F	Volume V_S	Depth Y_{max}	L_{fos}	W_{fos}	L_{scul}	W_{scul}	Shape
1	f–l	20.0	181.1	207.3	790.0	3.05	12.5	9.5	165	132	P
2	M–l	24.6	236.8	300.5	910.0	3.05	13.5	11.5	165	135	C
3	b–l	21.4	238.7	202.9	790.0	3.10	14.0	11.0	155	144	C
4	b–l	12.3	124.2	112.2	920.0	2.15	11.0	10.5	181	145	C
5	f–M	21.4	222.7	205.7	1190.0	3.00	13.5	11.0	175	147	C
6	b–r	17.1	165.4	119.9	1570.0	2.45	13.5	10.0	164	147	P
7	f–r	14.7	120.0	53.9	840.0	2.50	12.0	8.0	147	133	P
8	f–l	20.2	150.9	241.9	840.0	2.10	11.5	12.5	172	135	P
9	f–l	16.9	132.0	150.5	840.0	2.20	12.0	10.0	160	135	P
10	F–l	22.8	170.5	204.8	520.0	3.10	11.0	10.0	164	157	C
11	b–r	12.8	134.7	76.9	1160.0	1.90	13.5	10.5	175	145	P
12	f–	19.3	140.0	135.7	490.0	2.80	10.0	10.0	164	152	C
13	f–l	20.1	165.0	176.8	880.0	3.00	11.0	10.0	178	138	C
14	M–r	12.2	103.5	43.8	580.0	2.40	11.5	7.5	167	141	C
15	b–l	14.3	125.0	134.2	460.0	2.00	12.5	10.0	162	153	C
16	b–l	24.3	192.9	274.0	700.0	3.05	11.5	11.0	176	135	P
17	M–r	9.7	63.0	23.8	530.0	1.40	10.0	9.0	167	135	C
18	b–l	21.2	165.0	199.2	670.0	3.00	11.0	10.0	154	138	C
19	f–r	18.6	124.7	112.8	900.0	2.50	10.5	9.5	156	135	C
20	b–l	19.6	184.3	157.9	1120.0	2.60	13.5	10.5	188	143	P
MV	b–l	18.2	157.0	156.7	835.0	2.57	12.0	10.1	167	141	12C–8P

seal fossa. In order to better indicate its position, we divided the total length and total width of the fossa into quadrants, symbolised as F–f–b–B (from front to back) and L–l–r–R (from right to left). Thus capital letters indicate the quadrants more distal from the middle, while lower case letters indicate the quadrants adjacent to the middle of the fossa. The M stands for the cases in which the maximal depth lay within 0.5 mm from the middle. We noticed that in all cases but one the maximal depth lay within the quadrants adjacent to the middle and that its preferential half is the left one, in accordance with Lang and Tisch-Rottensteiner [15]. The use of the chi-squared test reveals that this preference is statistically significant.

The total area A ($= A_L + A_R$) of the frontal section of the fossa (Figs. 2, 3) is included in the third column. It ranges from 9.7 mm^2 to 24.6 mm^2 with a mean value (included in the last row as "MV") of 18.2 mm^2.

The fourth column comprises the volume of the fossa, calculated with the help of the simplified

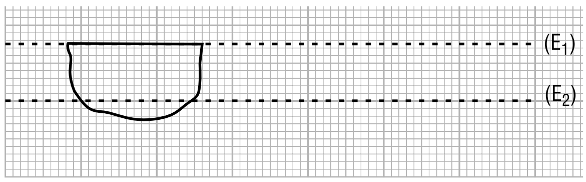

Figure 2. Outline of the anterior view of the frontal section of the cast of the *sella turcica* passing through its deepest point. As the cast of the hypophyseal fossa *per se* the part of the section below the level indicated by (E_2) was considered.

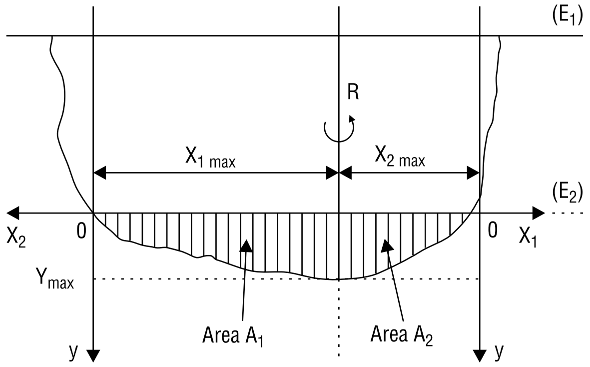

Figure 3. Magnification (5×) of Figure 2 so that a graph representing the change in depth (Y) of the fossa as a function of the distance from its right (X_1) or from its left (X_2) rim may be obtained. The axis of rotation *R* passes through the point that corresponds to the maximal depth (Y_{max}). A length of 2.5 mm in this graph represents 0.5 mm in the original section.

mathematical formula proposed by DiChiro and Nelson [10]: volume (V_{DN}) = 0.5 × (length) × (width) × × (depth), as this formula has also been used by other authors [16, 21]. The volumes thus evaluated range from 63 mm^3 to 238.7 mm^3 with a mean value of 157 mm^3.

The fifth column contains the volume of the fossa (V_F), calculated according to our methods (by Pappus' theorem). Our values range from 23.8 mm^3 to 300.5 mm^3 with a mean value of 156.8 mm^3. Apart from the (obviously incidental) coincidence of the mean values, they differ significantly from the one contained in the previous column. This fact is commented on below (see Discussion).

The total volume of the sella (V_S) (evaluated by simple immersion of the casts and ranging from 460 mm^3 to 1570 mm^3) occupies the next column and the maximal depth (within the fossa) the seventh column. It presents a minimum of 1.4 mm and a maximum of 3.1 mm.

In the eighth and ninth columns we present the length (L_{fos}) and the width (W_{fos}) of the fossa. We noticed a significant variation in the lengths, from 10.0 mm to 14 mm, or [(max – min)/min = 40%] and a greater one in the widths (from 7.5 mm to 12.5 mm or 66.7%). In order to examine a possible correlation between these dimensions and those of the entire skull, we performed measurements of the corresponding lengths L_{scul} and widths W_{scul}, included in the next two columns. The lengths present a variation from 154 mm to 188 mm (22%) and the widths a smaller one (from 132 mm to 157 mm or 18.9%). The appropriate statistical analysis (described in Materials and Methods) revealed no correlation between these values and the corresponding dimensions (L_{fos} and W_{fos}) of the hypophyseal fossa.

Lengths, areas and volumes were measured or calculated in mm, mm^2 and mm^3 respectively. Although the mathematical methods and our computer program permitted us an accuracy of three decimal places, we preferred to truncate the values to one decimal place, so that they corresponded with the volumes of the sella V_s (sixth column), for which no such accuracy was possible (and meaningful).

The last column includes information relevant to the shape of the fossa. Where 1/2 or more of the Y-values are identical (differences of 0.2 mm of less were not taken into account), we assumed that a "plateau" (P) was formed. Otherwise the structure was classified as being of "normal" concave (C) shape. We decided to consider a shape as "irregular" only if an alternation of "hills" and "valleys" occurred with a "hypsometrical difference" greater than 0.2 mm. No such shape was found. Concave shapes (12) prevail, as expected, over those with "plateau" shaped fossae (8).

Finally, the last line contains the mean values (MV) of the corresponding column. In its second column particularly the prevailing position of the maximal depth is indicated. The meaning of the content of its last column is obvious.

A review and a global appreciation of the most significant results are given below.

DISCUSSION

Our work was focused on the study of the hypophyseal fossa and not on the entire *sella turcica* (as these structures are clearly defined and have been distinguished in the Introduction). The reason for this is the shortage of references concerning this important part of the sella and the lack of published methods aimed at exact delineation of the fossa and the determination of its morphometric features. Indeed, the literature provides a sufficient number of reports on the length and width of the fossa (that may be considered as identical to those of the sella) but none on the depth and volume of the fossa itself. Still, the dimensions of the fossa are much smaller than those of the sella and direct measurement of its volume and depth might lead to important errors. This is the reason why we chose the geometrical method described above.

Since our sample is rather small compared to the number of specimens used by other authors, the comparison of our findings with those provided by the literature may be regarded as indicative only.

It is, nevertheless, indispensable, since it allows the validity of the proposed method to be assessed.

Several reports are available on the shape of the fossa, identified with the floor of the sella. A comparison can thus be made with our findings. What we found were 12 (60%) specimens with a normal concave shape of the fossa, 8 (40%) specimens with a plateau and no specimens of irregular shape. Our results are thus in fair accordance with Lang and Tisch-Rottensteiner [15], who found, respectively, 50%, 46% and 4%. If we class concave and plateau shaped fossae as "regular," we also agree with Ouaknine and Hardy [16] who reported 96% "regular" cases.

Our findings concerning the length (10 mm $\leq X_S \leq$ 14.0 mm, MV 12.0 mm) and width (7.5 mm $\leq X_T \leq$ 12.5 mm, MV 10.1 mm) conform to those of Camp [7] (length: 5–16 mm, MV 10.5 mm), Renn and Rhoton [21] (length: 7–14 mm, MV 10 mm; width: 10–16 mm, MV 13 mm) and Ouaknine and Hardy [16] (length: 6–16 mm, MV 10 mm; width: 7–17 mm, MV 13.5 mm). It is worth noticing that, in contrast to previous results, our study suggests that the length is, as a rule, greater than the width. In order to acquire any anthropological meaning, this finding needs to be confirmed by the use of a larger number of specimens. Moreover, it must be mentioned that the variability of the skulls of our sample does not suffice to account for that of the fossae, since the statistical analysis of our data showed no correlation between the dimensions of the hypophyseal fossae and those of the corresponding skulls.

With regard to the volume of the sella (V_S), it must be pointed out that if dry skulls are involved it is not necessary to use the mathematical formula of DiChiro and Nelson [10]: volume = 0.5 × (length) × (width) × × (depth), since the volume can easily be measured by immersion of its cast, as described above. Moreover, the shape of the sella may hardly be likened to an ellipsoid, the volume of which is supposed to be approximated by the formula in question. On the contrary, the sella resembles a superposition of a parallelepiped and an ellipsoid, the latter occupying exactly the volume of the fossa. Consequently, the adoption of the formula of DiChiro and Nelson [10] results in volumes much smaller than ours. The mean volume of the sella was evaluated as 594 mm^3 by DiChiro and Nelson [10] themselves, 621 mm^3 by Renn and Rhoton [21] and 575 mm^3 by Ouaknine and Hardy [16]. Our measurements yielded the much greater mean value of 835 mm^3.

According to our reasoning, the application of the formula of DiChiro and Nelson [10] in the evaluation of the volume of the fossa alone gives the same mean value (157.0 mm^3) as the mean value of the volume arising from the use of Pappus' theorem as in our method (156.7 mm^3). Nevertheless, there are important differences in the evaluation of each separate volume and we have every reason to believe that our approach is much closer to the actual volume, as it takes into account the peculiarities of each specimen.

Several clinical factors are able to influence the shape and the volume of the pituitary gland. Benign tumours of the anterior lobe of the hypophysis such as microadenomas (less than 10 mm in diameter) or macroadenomas (greater than 10 mm) are fairly common. These may secrete pituitary hormones such as prolactin, GH, ACTH, LH, FSH or TSH and thus be discovered by their clinical consequences. They may also remain non-secreting and latent, unless revealed incidentally or in the course of autopsy, although macroadenomas may elicit non-hormonal clinical manifestations by the exertion of pressure on neighbouring structures (such as the optic chiasm).

Other types of tumour readily recognisable by their eventually severe clinical repercussions (craniopharyngiomas, germinomas, dysgerminomas and gliomas) are fortunately rare. Inflammatory diseases such as sarcoidosis, tuberculosis, lymphocytic hypophysitis and histiocytosis-X are also possible [1].

Among these lesions, non-functioning microadenomas are the most frequent, reaching an incidence of the order of 10–20% [2]. Small interpituitary cysts may occur (usually in the *pars intermedia* of the gland) and are also capable of altering the total size of the pituitary.

A similar incidence (ranging from 5% to 23%) is ascribed to the very well known "empty sella syndrome". This situation is of non-pituitary origin, since it arises from a congenital incompetence of the *diaphragma sellae*, which induces an extension of the subarachnoid space into the sella, as well as a remodelling and enlarging of the latter and a flattening the pituitary gland. This situation may also remain asymptomatic.

Finally, it should be noted that a normal proliferation of the prolactin-secreting cells (or "lactotrophs") during pregnancy accounts for a twofold increase in gland size [2].

The hypophysis is thus regarded as an organ of the greatest variability in shape and/or in size. Consequently, variations in the *sella turcica* are also frequent, although they may be due to other relating structures as well (such as an aneurysm of the carotid artery). In particular, the shape of the hypophyseal fossa (floor of the sella) may also be affected by the local morphology of the dura and by the occurrence of intercavernous sinuses [21]. Simultaneous examination of the hypophysis and the surrounding sella was performed on excised specimens several decades ago in an attempt to associate clinical pituitary disorders with radiological findings, as X-rays were the only available means of *in vivo* imaging of the region in question. The advent and wide use of MRI techniques permitted direct *in vivo* visualisation of the pituitary and the hypothalamus and has been established as the current procedure of choice for the imaging of these organs. X-Ray examination of the sella has thus become obsolete for diagnostic purposes. Nevertheless, the study of cadaveric material has preserved its anatomical interest and the extent of the correlation between variations of the hypophysis and those of the *sella turcica* still remains a subject of controversy.

Burrow et al. [6] examined 120 sphenoid bones and pituitaries originating from autopsies and discovered only 6 cases in which the radiological findings were consistent with the actual existence of microadenomas. A further analysis of these results is given by Wortzman and Rewcastle [27], in which the asymmetry of the posterior lobe (13 cases) is recognised as the major cause of the 27/120 false positive results.

Banna et al. [4] performed multidirectional thin section tomographies on 62 excised sphenoid bones and histological examinations of their corresponding pituitaries and found no meaningful correlations between the radiological and the histological findings.

However, the use of MRI techniques *in vivo* did show such a correlation. Dietrich et al. [11] examined 42 patients with proven microadenomas and 42 healthy persons. They found that the normal pituitary glands had a lower volume (MV: 535 mm^3) than those with microadenomas (MV: 734 mm^3). Furthermore the healthy subjects presented less frequent anatomical variations in their hypophyses and corresponding sellae (10–21%) than those with microadenomas (48–71%).

These discrepancies may partly be explained by the fact that the more frequent microadenomas with a diameter lower than 5mm do not usually alter the normal pituitary contour [2]. The position of the adenoma is also relevant. Adenomas produced by cells located at the lateral portion of the anterior lobe (as is usual in the case of somatotrophs) are less likely to have an impact on the neighbouring parts of the sella.

MRI techniques may permit the application of our numerical methods in assessing the geometrical features of the *sella turcica* and the hypophyseal fossa *in vivo*, provided that imaging is performed in the sagittal and frontal planes at intervals of 0.5 mm. Nevertheless, more subtle methods exploiting knowledge from analytical geometry and sophisticated algorithms and computer programming (see, for example, [12]) may provide neurosurgeons with all the required information concerning the best approach to a pituitary tumour or adenoma that is to be resected.

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